Blisters, crusts and lines – an infant with a hereditary skin disorder

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Title image (source: Wikipedia):
Alfred Blaschko (1858-1922), German dermatologist

A female infant was delivered by repeat Caesarean section at 39 1/7 weeks of gestation to a 25-year-old G3/P2 following an uneventful pregnancy at another institution. The first child was a healthy two-year-old boy; the second pregnancy had ended in early abortion. The parents, originally from Somalia, have been living in Switzerland for 2 years. The mother had a history of acute Hepatitis B (in remission), allergic asthma and hypothyroidism. The family history was otherwise unremarkable.

The newborn had an umbilical cord pH of 7.33 and adapted well with an Apgar score of 8, 9, and 9 at 1, 5 and 10 minutes, respectively. Physical examination at birth revealed a disseminated exanthem with multiple vesicles, pustules and brown macules covering the entire body, but excluding the palms of the hands, soles of the feet and the head. The infant was referred to the Neonatal Intensive Care Unit (NICU) of the University Hospital of Zurich for further care and investigations.

On admission to the NICU, the baby was found to be in excellent condition. The skin lesions consisted of pustules, multiple hyperpigmented lesions, some of them very large and surrounded by a white collarette (Fig.1, 2). On the chest and abdomen, the lesions appeared in a curvilinear pattern, whereas on the extremities the lesions were linear, following the lines of Blaschko (Fig. 3).

The palms, soles and head were spared. The remainder of the physical examination was normal.

The initial differential diagnoses made by the neonatologists included transient neonatal pustular melanosis, incontinentia pigmenti and infectious exanthem. Swabs were taken from the skin lesions to rule out bacterial or viral infection. The bacterial culture showed skin flora with coagulase-negative staphylococcus and staphylococcus aureus. PCR was negative for viral DNA.

On day 2 of life, the child was seen by a pediatric dermatologist who also found the clinical picture to be highly characteristic of incontinentia pigmenti (IP). A skin biopsy obtained on day 3 of life showed a normal stratum corneum, small intraepidermal neutrophilic abcesses, eosinophilic spongiosis and a few apoptotic keratinocytes in the epidermis. The dermis revealed perivascular inflammatory infiltrates consisting of lymphocytes, histiocytes and eosinophilic granulocytes (Fig. 4, 5). These histopathologic findings confirmed the diagnosis of IP, versicular stage. The skin lesions were treated with a daily bath in Antidry almond oil for ten minutes to prevent drying. This was followed by local application of a disinfectant, Triclosan 1% on the entire body.

The family history regarding IP was negative. However, examination of the mother showed very discrete, hypo-

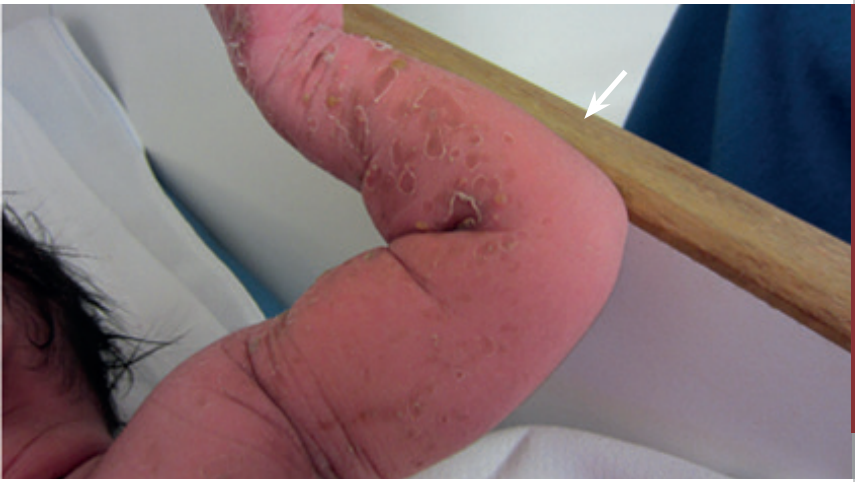

Fig. 1

Admission to the NICU on DOL 1: few pustules and brown maculae with white collarette arranged linearly on arm and hand.

Fig. 2

Skin changes on left leg (DOL 2): vesicles, pustules and brown maculae in linear formation following the lines of Blaschko.

Fig. 3

Skin lesions on chest and abdomen (DOL 3):
Curvilinear lesions following the lines of Blaschko.

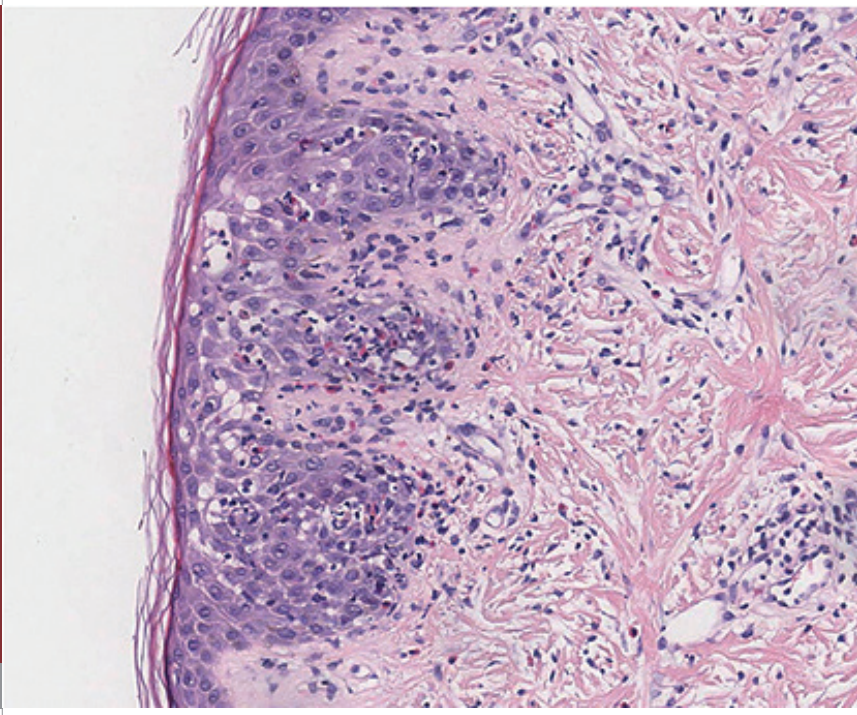

Fig. 4

Skin biopsy (low magnification): normal stratum corneum, small intraepidermal neutrophilic abcesses, eosinophilic spongiosis and a few apoptotic keratinocytes in the epidermis. The dermis revealed perivascular inflammatory infiltrates consisting of lymphocytes, histiocytes and eosinophilic granulocytes.

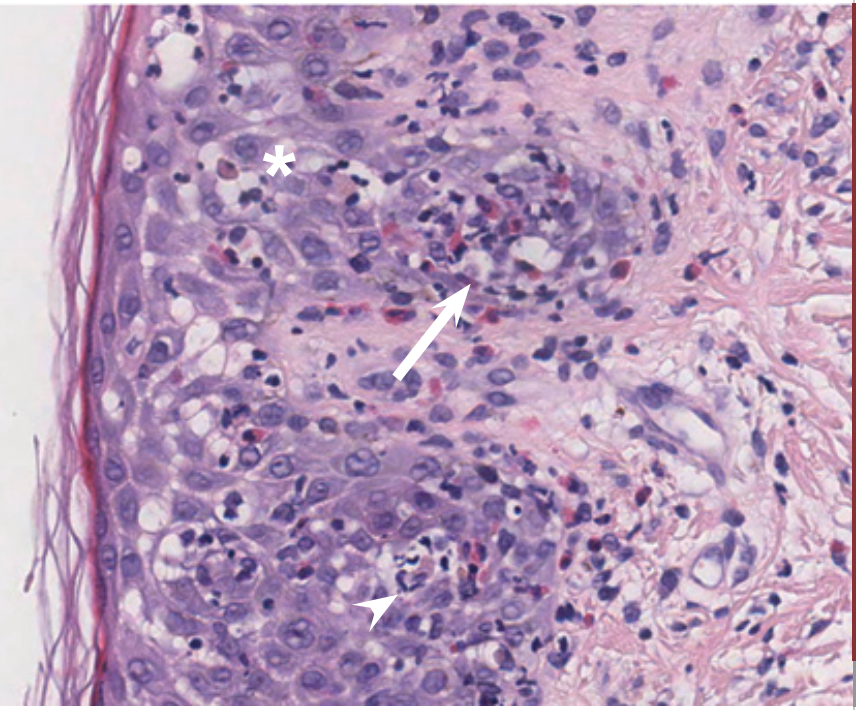

Fig. 5

Skin biopsy (high magnification): neutrophilic abscesses (arrow head), eosinophilic spongiosis (arrow), apoptotic keratinocytes (asterisk).

Fig. 6

Symptoms of female ancestors can be quite discrete and limited to the skin.

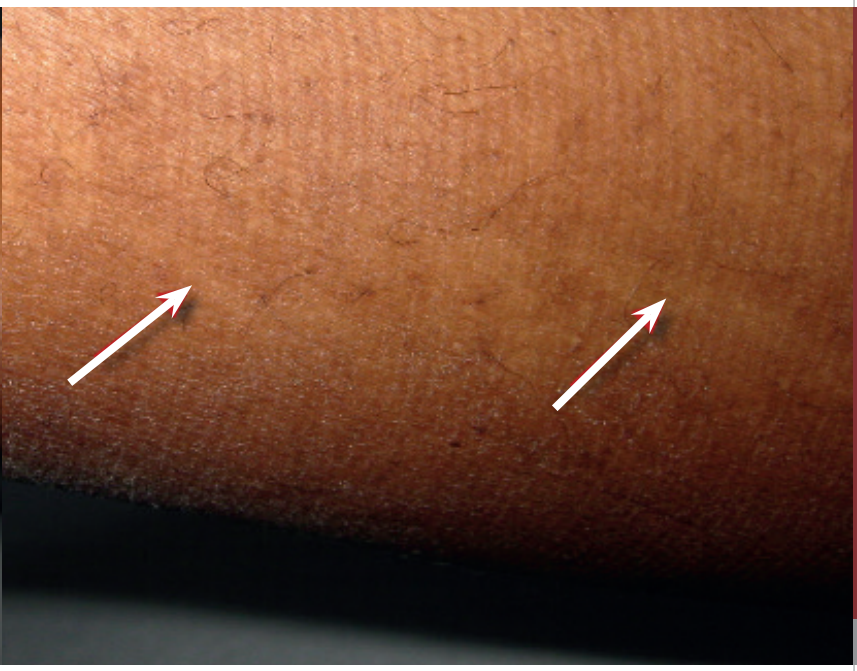

Fig. 7

Maternal skin changes: Linear hypopigmented streaks on leg of the mother (arrows).

pigmented striae on her legs, possibly representing healed lesions of IP (Fig. 6, 7).

Neurologically, the girl showed no obvious symptoms, no seizures were observed and a cerebral ultrasound examination was normal. An ophthalmological examination revealed normal retinal vessels and normal vascularization. The infant was transferred to the maternity ward on the third day of life and discharged home on the sixth day of life. At this point, most of the lesions were crusted (Fig. 8, 9).

At follow-up in the dermatological clinic at the age of 1 month, the crusts and hyperkeratotic lesions had healed and been replaced by hyperpigmented macules, still neatly assembled along the Blaschko lines. Otherwise, the girl showed no other signs of the illness, and she was neurologically normal and thriving. At the age of 13 weeks, a repeat ophthalmological examination did not reveal any abnormalities.

Following a viral gastroenteritis at the age of 12 weeks, the infant again developed streaky lesions with erythema at the borders of both hands. The lesions seemed to be itchy and developed crusts, which fell off after some days. At dermatological follow-up, the infant showed slightly atrophic hyperpigmented areas on the back of the hands. Hyperpigmented lesions along the lines of Blaschko were still visible all over the body excluding the palms, soles and the head. The episode

Fig. 8

Skin lesions on DOL 5: most lesions are crusted or erythematous.

Fig. 9

Skin lesions on DOL 5: crusts are falling off, leaving hyperpigmented or erythematous skin lesions.

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is an uncommon hereditary multisystem disease. The incidence is approximately 1:10'000-100'000 (1). Inheritance is X-linked dominant. In general, only females are affected, as affected males die during early pregnancy (2). Other affected family members can only be found in 30-50% of the cases, and symptoms in female ancestors can be quite discrete, limited to the skin and go unnoticed (2). This was also the case in our patient's mother, where the only evidence for IP were linear streaks of hypopigmentation on her legs.

The genetic background of IP has been well known since 2000. The IP locus is linked to the Factor-VIII-gene in the region Xq28 (3). The cause of IP is a mutation in the NEMO/IKK-γ-gene. This affects an important factor in the signaling pathway of nuclear factor-kappa-B, which plays an important role in immunologic, inflammatory and apoptotic processes (4).

The characteristic skin lesions are present at birth in approximately 50% of cases and follow the lines of Blaschko. These are also known as cutaneous lines of embryogenesis as they apparently trace the migration of embryonic cells. The skin lesions develop in four phases (2): in the first stage, one can observe inflammatory lesions consisting of reddish streaks and blisters; these can persist until the child is 4 weeks old. The second phase shows hyperkeratosis with incrusted,

thicker, sometimes wart-like (verrucous) lesions from the fourth week onward until the sixth month of life. This phase changes to the third stage, showing more and more hyperpigmented spots and stripes. At school age and in puberty, the lesions then alter into areas of hypopigmentation with atrophy of the affected regions of the skin. The stages may overlap in time and can also occur in utero so that vesicular lesions may be seen along with verrucous or hyperpigmented lesions at birth, as was the case in our baby.

IP belongs to the group of the ectodermal dysplasias. Apart from the skin, other structures of ectodermal or mesenchymal origin can be affected. Hence, patients with IP show anomalies of the teeth in 80% of cases (5) (delayed tooth development, partial anodontia, conical teeth, enamel-disorders), nail-dystrophy in 7-40% (5), vertex alopecia in 38% (2), ophthalmologic complications in up to 35% (2) (e.g. vaso-occlusive retinal events leading to retinal detachment and loss of vision) and neurologic complications (mental retardation, seizures, spastic diplegia) in approximately 30% of cases (1). Infants with eye problems are more likely to have neurologic problems (6).

In general, IP has a good prognosis, as long as there are no severe ophthalmologic or neurological complications. If seizures occur within the first weeks of life, the infant is at risk for mental retardation and should have neurodevelopmental follow-up (7). In the

first year of life, ophthalmologic examinations every 3 months are recommended. Dental or maxillofacial surgery may be needed in the course of the patient's life.

CONCLUSION

We report the case of a female infant presenting with the classical skin manifestations of IP at birth. The differential diagnoses in the early blistering phase include transient neonatal pustular melanosis, infections (bacterial or viral) and diffuse cutaneous mastocytosis. The diagnosis of IP can be confirmed by skin biopsy. As IP is a multisystem disease most commonly involving the eyes and central nervous system, management includes baseline and regular ophthalmological and neurological examinations in the early years of life. In the acute stage with blisters, inflammation and crusts, local skin care with antiseptic creams (e.g. containing triclosan 1%) is recommended. In more severe cases, mild topical steroids may be applied as well. In the absence of neurological or ophthalmological complications the prognosis is good.

See also: COTM August 2007.

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